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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

EWOLDT, GERALD R

ART UNIT PAPER NUMBER

1644

DATE MAILED: 02/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/854,248

Applicant(s)

SALGALLER ET AL.

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10,12-21 and 36-43 is/are pending in the application.
- 4a) Of the above claim(s) 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10,12-21 and 36-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 1/10/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks, filed 1/10/05, have been entered.

2. Claim 15 stands withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 10-14, 16-21, and newly added Claims 36-43 are being acted upon.

3. Upon reconsideration, all previous rejections have been withdrawn. The following are new grounds for rejection.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 10-14, 16-21, and newly added Claims 36-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,788,963 (1998, IDS) in view of Thurnher et al. (1997, IDS) and Ramoner et al. (1998, IDS).

The '963 patent teaches a method for producing an anti-tumor cell, antigen specific cytotoxic T cell (CTL) response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1) derived from various sources including tumor cell lysates and purified antigens (see particularly column 8, PROSTATE SPECIFIC ANTIGENS FOR PRESENTATION BY DC). The reference further teaches that the DCs are obtained from peripheral blood, have been cryopreserved, have been obtained from a healthy HLA matched donor, are extended life span, and can be administered to a metastatic prostate cancer patient (see particularly the Claims).

The reference teaching differs from the claimed invention only in that it does not teach the use of BCG in the *in vitro* exposure of the DCs to antigen.

Thurnher et al. teaches the *in vitro* maturation and activation of DCs with BCG (see particularly pages 129-130, RESULTS, *BCG mycobacteria induce maturation of DCs*). The reference further teaches that DCs matured in the presence of BCG may also take up tumor antigens and thus, then be capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response (see particularly page 131, DISCUSSION). The reference concludes by teaching tumor-antigen loading of DCs cultured in BCG (see particularly page 133, column 2).

Ramoner et al. further extends the work of Thurnher et al. The reference teaches that BCG "is a potent activator of human DCs." The reference further teaches that BCG stimulates the ability of DCs to activate T cells. The reference further teaches that BCG could be used in DC based tumor immunotherapy (see particularly page 1491, CONCLUSIONS).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method for producing an anti-tumor cell, antigen specific CTL response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1), said DCs having been obtained from peripheral blood, having been cryopreserved, having been obtained from a healthy HLA matched donor, having been extended life span, and having been administered to a metastatic prostate cancer patient, as taught by the '963 patent. One of ordinary skill in the art would have been motivated to add BCG to the *in vitro* exposure of DCs to antigen for an improved anti-tumor, antigen specific CTL response, given the combined teachings of Thurnher et al. and Ramoner et al. that: 1) BCG causes the maturation of DC and thus, the DCs are then capable of activating tumor-reactive T cells in a cytokine milieu that favors the generation of a strong anti-tumor CTL response and 2) BCG "is a potent activator of human DCs", BCG stimulates the ability of DCs to activate T cells, and BCG could be used in DC based tumor immunotherapy. Regarding Claims 36 and 40, said claims comprise only the routine optimization of the claimed method and fall well within the purview of one of ordinary skill in the art at the time of the invention.

Applicant's arguments, filed 1/10/05, in traversal of a similar rejection, have been fully considered but they are not persuasive. Applicant argues that the new limitation to the claims, i.e., a method for producing an antigen specific CTL response, distinguishes the claimed method from the prior art. Applicant argues, "Ramoner et al. do not disclose or suggest the use of BCG, or BCG and LPS, combined with an antigen can promote a MHC-class 1 response" and "Ramoner et al. only suggest generally the use of BCG in dendritic cell based immunotherapy. There is no suggestion or detailed enablement of how BCG might be used, such as for example, combined with DCs at the time of administration or subsequent to administration as an adjuvant for an *in vivo* response, or in some other manner". Applicant concludes, "Applicants do not believe that Ramoner et al. provide any motivation to combine DCs, an antigen and BCG in the manner recited in the pending claims. Further, Ramoner et al. neither alone or in combination with U.S. Patent 5,788,963 explicitly suggest the claim element that is the difference between the claimed invention and the prior art".

Applicant is advised that the prior art need only render obvious the actual method of the claims. Also, the motivation to combine references need not be the same as the motivation of the Applicants. In the instant case the claims recite only the administration of DCs after *in vitro* exposure of said DCs to antigen and BCG. The primary reference teaches the administration of DCs after *in vitro* exposure of said DCs to antigen. The secondary references teach several reasons why the ordinarily skilled artisan would include BCG in the antigen exposure step, e.g., BCG exposure induces a cytokine milieu that favors the generation of a strong anti-tumor CTL response. Accordingly, Applicant's additional reasons for including BCG in the antigen exposure step, e.g., producing an antigen specific CTL response, comprise only Applicant's reasons for performing an already obvious method.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 36-43 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does

not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) the generic method of Claim 36 comprising simultaneously combining antigen, BCG, and DCs.

B) the generic method of Claim 40 comprising contacting antigen with DCs subsequent to contact of DCs with BCG.


Applicant indicates that support for this new limitations can be found at pages 29 and 31. The support Applicant has indicated is not disclosed in the generic context as claimed. Applicant has cited Examples 1 and 2 which disclose specific experiments employing specific parameters, e.g., specific concentrations of reagents, specific antigens, etc. Such disclosures provide insufficient support for the generic methods of the claims.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

10. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

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2/15/05
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